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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/664,341	09/16/2003	Alexey Zdanovsky	341.021US1	4133
21186 7590 06/01/2009 SCHWEGMAN, LUNDBERG & WOESSNER, P.A. P.O. BOX 2938 MINNEAPOLIS, MN 55402			EXAMINER PAK, YONG D	
			ART UNIT 1652	PAPER NUMBER
			NOTIFICATION DATE 06/01/2009	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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uspto@slwip.com
scape@slwip.com

Office Action Summary	Application No. 10/664,341	Applicant(s) ZDANOVSKY ET AL.	
	Examiner YONG D. PAK	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 January 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-23 and 25-46 is/are pending in the application.
- 4a) Of the above claim(s) 12-14, 21-23, 26-29, 33, 38-40, 45 and 46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11, 15-20, 25, 30-32, 34-37 and 41-44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The amendment filed on January 12, 2009, amending claims 1-3, has been entered.

Claims 1-23 and 25-46 are pending. Claims 12-14, 21-23, 26-29, 33, 38-40 and 45-46 are withdrawn. Claims 1-11, 15-20, 25, 30-32, 34-37, and 41-44 are under consideration.

Election/Restrictions

Claim 17 is partially directed to non-elected inventions SEQ ID NOs:47, 48, 49, 66, 69-71 and 73-80. For examination purposes, the Examiner will only examine the elected invention, polynucleotide comprising SEQ ID NO:72.

Response to Arguments

Applicant's amendment and arguments filed on January 12, 2009, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112 – 2nd paragraph

In view of the amendment of claim 1 deleting the term "complementing", the rejection of claim 1 and claims 4-11, 17-19, 25, 30-31, 35-37, and 41-44 depending

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therefrom under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been **withdrawn**.

Claim 1 and claims 4-11, 17-19, 25, 30-31, 35-37, and 41-44 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the phrase “enhanced protein degradation”. The metes and bounds of this phrase in the context of the above claims are not clear to the Examiner. It is not clear to the Examiner as to how much of an increase protein degradation is considered as “enhanced protein degradation” by the applicants. A perusal of the specification did not provide a clear definition for the above phrase. Without a clear definition in terms of numerical value, those skilled in the art would be unable to conclude what is “enhanced protein degradation”.

Claim Rejections - 35 USC § 112-1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In view of the amendment and arguments, the rejection of claims 1-11, 15-16, 18-20, 25, 30-32, 34-37, and 41-44 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, has been **withdrawn**.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Applicant's arguments, see pages 13-14 of the Remarks, filed January 12, 2009, with respect to the rejection(s) of claim(s) 1-11, 15-20, 25, 30-32, 34-37, and 41-44 under 35 U.S.C. 103(a) as being unpatentable over Leclerc et al., Corish et al., Gilon et al. and Kastelic et al. have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Daly.

Claims 1-11, 15-20, 25, 30-32, 34-37, and 41-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daly and Gilon et al.

Claims 1-11, 15-20, 25, 30-32, 34-37, and 41-44 are drawn to (A) a fragment of SEQ ID NO:72 which encodes a polypeptide with substantially the same activity as the full-length fusion polypeptide encoded by SEQ ID NO:72 or (B) a polynucleotide encoding a fusion polypeptide comprising a luciferase and a PEST protein destabilization sequence or a protein destabilization sequence of SEQ ID NO:89 and/or an AU-rich mRNA destabilization sequence and further comprising an inducible promoter and a vector and host cell comprising said polynucleotide, wherein the half life of expression of luciferase is 20 or 30 minutes or said fusion polypeptide has an enhanced protein degradation relative to a fusion polypeptide comprising only one of the protein destabilizing sequence.

Daly (US Patent No. 7,157,272 – form PTO-892) discloses a polynucleotide encoding a reporter protein, such as a luciferase, one or more protein destabilizing sequences, such as including a PEST sequence from mODC and a N-terminal

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degradation signal for ubiquitin system proteolysis, and one or more mRNA destabilizing sequences, such as an AU rich mRNA destabilizing sequence, wherein said destabilizing sequences are C-terminal to the reporter protein, wherein said fusion polypeptide has an enhanced protein degradation relative to a fusion polypeptide comprising only one of the protein destabilizing sequence, and wherein the half-life is about 20-30 minutes (Column 16, lines 18-67, Column 26, lines 36-59, Column 54, line 57 through Column 55, line 20). Daly also discloses vectors comprising inducible/repressible promoters operably linked to the above polynucleotide and optimization of the above polynucleotide optimized for expression in eukaryotic cells (Column 5, line 65 through Column 6, lines 59 and Column 22, line 7 through Column 23, line 46). Daly discloses that the combination of mRNA destabilization and protein destabilization significantly improves the reporter levels or activity in expression constructs compared to constructs without destabilization elements or with only one type of destabilizing element since protein destabilizing elements reduce the intracellular half-life of a protein and mRNA destabilizing sequences reduce the intracellular half-life of RNA transcript (Column 26, lines 2-24). Daly provides several protein destabilizing sequences, such as ubiquitin, or variant or derivative of ubiquitin or protein degradation signals and several mRNA destabilizing sequence and that multiple combinations can be used (Column 25, lines 39-40, Column 30, lines 13-14, and Column 53, lines 35-38).

The difference between the reference of Daly and the instant invention is that Daly does not teach a polynucleotide encoding a fusion protein comprising the CL1

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protein destabilizing sequence of SEQ ID NO:89, which is a C-terminal degradation signal for ubiquitin based proteolysis.

Gilon et al. (form PTO-1449) discloses several protein destabilizing sequence, such as a CL1 sequence (ACKNWFSSLSHFVIHL) which is 100% identical to the CL1 sequence of SEQ ID NO:89, attached C-terminal to the protein of interest and promotes degradation of the protein (See Table 1 on page 2763 of Gilon et al. and on page 31 of the instant specification).

Therefore, in combining the teachings of Daly and Gilon et al., it would have been obvious to one having ordinary skill in the art to add an additional protein destabilizing sequence of Gilon et al. to the construct of Daly or to substitute the N-terminal degradation for ubiquitin. One of ordinary skill in the art would have been motivated to add the protein destabilizing sequence of Gilon et al. or to substitute the N-terminal degradation signal of Daly with the C-terminal degradation signal of Daly in order to further reduce the half life activity/expression of luciferase comprised in the fusion protein of Daly. One of ordinary skill in the art would have had a reasonable expectation of success since Daly teaches reducing the half-life of a reporter protein such as a luciferase by using multiple destabilizing sequences and Gilon et al. teaches a C-terminal degradation signal for ubiquitin based proteolysis which reduce.

Therefore, the above references render claims 1-11, 15-20, 25, 30-32, 34-37, and 41-44 *prima facie* obvious to one of ordinary skill in the art.

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

/Yong D Pak/
Primary Examiner, Art Unit 1652